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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,208	07/20/2001	Jiro Hitomi	MM4454	4894

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

MAIL DATE	DELIVERY MODE
11/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/910,208	HITOMI ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/04/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-26* is/are pending in the application.

4a) Of the above claim(s) *24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/4/06 has been entered.

2. Claims 18-26 are pending.

3. Claim 24-26 is withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention. Newly submitted claims 25-26 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The DNA encoding a calcium-binding protein of SEQ ID NOS: 19 or 20 is distinction from the claimed antibodies of claims 18-23. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 25-26 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. Claims 18-23 are under consideration in the instant application as they read on an antibody with binding affinity to a protein encoded by SEQ ID NO: 12.

5. Applicant request that the claims to be made part of interference No. 105,501, between US 5,976,832 and US application No. 08/761,289. The Examiner notes that judgment on the interference was made on 7/26/07.

6. The amendment filed 3/27/07 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment filed on 3/27/07 to the computer readable form of the "Sequence Listing" with SEQ ID NO: 19 and 20 represents a departure from the specification and the claims as originally filed. Applicant does not point out for support for the newly added sequences. It is noted that the new SEQ ID NO: 19 contains ^{17}Glu, which was not found in original SEQ ID NO: 19 (^{17}Gln). Further, new SEQ ID NO: 20 contains ^{65}Asn, which was not found in original SEQ ID NO: 20 (^{65}Gln). The specification and the claims as originally filed have no support for the new replacement of SEQ ID NO: 19 and 20.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 18-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrases "SEQ ID NO: 19 or 20) claimed in claims 18 and 21 and "these lineages" claimed in claim 22, line 3 represents a departure from the specification and the claims as originally filed.

Applicant's amendment filed 3/27/07 and 12/4/06 does not point to the specification for support for the newly added limitations "SEQ ID NO: 19 or 20" claimed in claims 18 and 21 and "these lineages" as claimed in claim 22. It is noted that the new SEQ ID NO: 19 contains ^{17}Glu, which was not found in original SEQ ID NO: 19 (^{17}Gln). Further, new SEQ ID NO: 20 contains ^{65}Asn, which was not found in original SEQ ID NO: 20 (^{65}Gln). However, the specification does not provide a clear support of such limitation. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.

9. Claim 22 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody with binding affinity to a calcium-binding protein comprising an amino acid sequence encoded by SEQ ID NO: 1 or 12 for diagnosing inflammatory diseases, dermatosis and lung and skin cancer, a method for producing a monoclonal antibody, and a calcium-binging protein assay regent comprising said antibody; does not reasonably provide enablement for a diagnostic agent for inflammatory diseases, "neoplastic diseases", dermatosis or "blood diseases of PMN, macrophages" and these lineages, which comprises an antibody of claim 18, in claim 22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Actions.

Applicant's arguments, filed 12/4/07, have been fully considered, but have not been found convincing.

Applicant indicates that a separate paper will be enclosed by the Applicants in the form of a Declaration to support enablement for claim 22.

Until said declaration is provided to show that claimed 22 is enabled for the claimed conditions, the rejection of claim 22 is maintained.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 18-19 and 22-23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Guignard *et al* (European Journal of Clinical Investigation, Vol:24, Supl. 2, pp.211, 1994), as is evidenced by Guignard *et al* (July 1995), Yamamura et al and the specification on page 2 lines 7-35.

Guignard et al (l 994) teach a polyclonal antibody (anti-P8 or anti-MRP-8), identify an unknown protein of 6.5 kDa (P6). Guignard et al also teaches that the P6 protein identified by N-terminal amino acid sequence analysis appeared to be a new protein of the S100 family (calcium-binding proteins). Further, Guignard et al concluded that a new protein of 6.5 kDa belonging to the S 100 family was evidenced in human neutrophils (see abstract in particular). While the Guignard et al is silent as to the "amino acid which is substantially identical to amino acid sequence listed in SEQ ID NO: 12" per se; P6 has the same N-terminal amino acid sequence encoded by SEQ ID NO: 12 as is evidenced by Guignard et al (1995) that the p6b N-terminal sequence (p6b) TKLEEHLEGIVNIFHQYSVR (see Figure 3, at page 398 in particular) which is 100% identical to amino acids 2-21 of the amino acid encoded by SEQ ID NO: 12. Further evidence that the amino acid sequence encoded by SEQ ID NO: 12 is p6 protein came from Yamamura et al who teach that Guignard et al (1995) isolated and partially characterized a novel human calcium-binding protein that cross-reacted with an antibody against MRP8. Yamamura et al concluded that the identified N-terminal 20 amino acid sequence of the reported protein was identical to that of human CAAF1, suggesting that this protein is CAAF1 (encoded by SEQ ID NO: 12) (see page 359, lines 4-8 in particular). SEQ ID NO: 12 encodes human CAAF1 as is evidenced by the specification on page 2, lines 7-35 that the human calcium-binding protein is CAAF1 encoded by SEQ ID NO: 12. The reference teachings anticipate the claimed invention.

12. Claim 18-20 and 22-23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Kelly *et al* (J. Patho. 1989), as is evidenced by Guignard *et al* (Immunol Cell Biol. 1996 Feb;74(1):105-7), Guignard *et al* (July 1995) Yamamura et al and the specification on page 2 lines 7-35.

Kelly et al teach monoclonal antibodies to study the expression of calgranulins by keratinocytes in inflammatory dermatoses. Kelly et al also teach that calgranulins are intracellular calcium binding proteins which have inflammatory cytokine activity. Further, Kelly et al teach that MAC 387 monoclonal antibody that recognizes a molecule probable containing both calgranulin A and B (see abstract in particular). MAC 387 monoclonal antibody also binds amino acid sequence encoded by SEQ ID NO: 12, as is evidenced by Guignard et al (Feb 1996) that the immunoreactivity of MAC 387 was compared with that of a polyclonal antibody raised against purified MRP-8, but cross-reacting with MRP-14, and p6, a novel S100 protein. Under such conditions, Mac 387 was found to recognize the three S 100 proteins (see abstract in particular). P6 has the same N-terminal amino acid sequence encoded by SEQ ID NO: 12 as is evidenced by Guignard et al (1995) teaches the p6b N-terminal sequence (p6b) TKLEEHLEG1VNIFHQYSVR (see Figure 3, at page 398 in particular) which is 100% identical to amino acids 2-21 of the amino acid encoded by SEQ ID NO: 12.

Further evidence that the amino acid sequence encoded by SEQ ID NO: 12 is p6 protein came from Yamamura et al who teach that Guignard et al (1995) isolated and partially characterized a novel human calcium-binding protein that cross-reacted with an antibody against MRP8. Yamamura et al concluded that the identified N-terminal 20 amino acid sequence of the reported protein was identical to that of human CAAF 1, suggesting that this protein is CAAF 1 (encoded by SEQ ID NO: 12) (see page 359, lines 4-8 in particular). SEQ ID NO: 12 encodes human CAAF1 as is evidenced by the specification on page 2, lines 7-35 that the human calcium-binding protein is CAAF1 encoded by SEQ ID NO: 12. The reference teachings anticipate the claimed invention

Applicant's arguments, filed 12/4/07, have been fully considered, but have not been found convincing.

Applicants submit there is no teaching in either reference of an antibody which is "specific to a calcium-binding protein comprising an amino acid sequence shown in SEQ ID. No. 19 or 20, or encoded by a nucleic acid sequence shown in SEQ ID NO: 1 or 12." Nowhere is there any teaching of a nucleic acid or amino acid sequence in either Guignard or Kelly nor has the Examiner made any allegation of teaching of the sequences. Both references just describe the antibodies and proteins, but nowhere is there any mention of the antibodies specific to the respective sequences. The Examiner uses Yamamura to help support the argument, and while it is not being relied on for the actual anticipation rejection, the reference itself is from 1996. Applicants point out that this application claims priority to its parent which issued as US 5,976,832 and was filed on December 6, 1995 which ultimately claims priority to JP 7-045564 and JP 7-070468 were filed on March 6, 1995. Therefore, Applicants believe that Yamamura cannot be used as a reference under this section of the statute.

Moreover, SEQ ID Nos. 19 and 20 have been found both novel and nonobvious as evidenced by US Patent No. 5,976,832, which is the parent to this application. Therefore, because the sequences underlying claims 18-23 are novel and nonobvious, Applicants submit that claims 18-23 of this application are also novel and nonobvious.

However, the disclosure of the sequences is only further characterization of otherwise known product. Actually, Guignard et al (l 994) and Kelly *et al* (J. Patho. 1989) are in possession of antibodies that binds SEQ ID NO: 12 because they teach antibodies that bind P6 (CAAF 1). That is they teach antibodies that bind a protein that is identical to the claimed CAAF 1. The Yamamura et al reference is provided only to show that a charactereistic non disclosed in the reference is inherent. Yamamura is an evidence that used to show an inherent characteristic of the P6 taught by the Yamamura reference is the claimed CAAF1 protein of SEQ ID NO: 12. Such evidence makes clear that the missing descriptive matter is necessarily present in the P6 protein described in the Yamamura et al reference, and that it would be so recognized by persons of ordinary skill. See *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 Fed. Cir. 1991). Also note that the critical date of extrinsic evidence, Yamamura et al, showing a universal fact need not antedate the filing date. See MPEP § 2124. Yamamura et al is only evidentiary reference and is not part of the rejection. The evidentiary

references need not to have an early dated of the claimed invention but can be post dated references.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guignard *et al* (European Journal of Clinical Investigation, Vol:24, Supl. 2, pp.211, 1994), as is evidenced by Guignard *et al* (July 1995), Yamamura et al and the specification on page 2 lines 7-35 in view of U.S. Pat. No. 5,654,403.

The teachings of Guignard et al have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of a method for producing a monoclonal antibody comprising the steps of culturing a hybridoma, and recovering the monoclonal antibody from the culture in claim 21.

However, it has been held that once the antigen of interest is selected, the use of that antigen in the known method of Kohler and Milstein will result in the expected hybrid cell lines and the specific monoclonal antibodies. Ex parte Erlich, 3 USPQ2d 1.011, 1015 (BPAI 1986).

The `403 patent teaches that a major step forward occurred in 1975 when Kohler and Milstein reported the successful fusion of spleen cells from mice immunized with an antigen with cells of a murine myeloma line. The resulting hybrid cells, termed hybridomas, have the properties of antibody production derived from spleen cells and of continuous growth derived from the myeloma cells. Each hybridoma synthesizes and secretes a single antibody to a particular determinant of the original antigen. To ensure that all cells in a culture are identical, i.e. that they contain the genetic information required for the synthesis of a unique antibody species, the hybridomas resulting from cell fusion are cloned and subcloned. In this way, the cloned hybridomas produce homogeneous or monoclonal antibodies. The '403 patent teaches that the advantages of hybridoma technology are profound. Because many hybrids arising from each spleen are screened for their potential to produce antibodies to the antigen of interest and only a few are selected, it is possible to immunize with impure antigens and yet obtain specific

antibodies. The immortality of the cell line assures that an unlimited supply of a homogeneous, well-characterised antibody is available for use in a variety of applications including in particular diagnosis and immunotherapy of pathological disorders (see col., 1, lines 41-57 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce monoclonal as taught by the "403 patent using the P6 protein taught by Guignard et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because such method will obtain specific antibodies. The immortality of the cell line assures that an unlimited supply of a homogeneous, well-characterised antibody is available for use in a variety of applications including in particular diagnosis and immunotherapy of pathological disorders as taught by the `403 patent.

Given the high sequence identity/homology between the referenced/claimed polypeptides; the resultant antibodies would have the inherent property of binding the claimed human CAAF1 of SEQ ID NO: 12 in the absence of objective evidence to the contrary.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was primafacie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 13, 2007

Maher Haddad

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